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10/567,570	10/18/2006	Antonello Covacci	002441.00190	2536

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EXAMINER	
TONGUE, LAKIA J	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,570	COVACCI, ANTONELLO	
	Examiner	Art Unit	
	LAKIA J. TONGUE	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *4-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/8/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-3, drawn to a *Streptococcus pneumoniae* bacterium in which expression of one or more gene has been knocked out.

Group II, claim(s) 4 and 8, drawn to a process for determining whether a test compound down-regulates expression of a target polypeptide.

Group III, claim(s) 5 and 6, drawn to a process for determining whether a test compound binds to a target polypeptide.

Group IV, claim(s) 7, drawn to a compound obtainable by the process for determining whether a test compound binds to a target polypeptide.

Group V, claim(s) 9 and 10, drawn to a compound obtainable by a process for determining whether a test compound down-regulates expression of a target polypeptide.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Pursuant to 37 C.F.R. 1.475(d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first recited **composition**, a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out.

Further pursuant to 37 C.F.R. 1.475(d), the ISA/US considers that any feature which the subsequently recited methods share with the main invention does not constitute a special technical feature within the meaning of PCT rule 13.2 and that each of such methods accordingly defines a separate invention.

Additional Election Requirement Applicable to All Groups

Regardless of which group is elected, a further election of invention is required.

Groups I-V, detailed above, read on patentably distinct and specific knock out genes. Consequently, Applicant is required to elect a specific gene. Each gene is patentably distinct because they possess differing biochemical and immunological properties and a further restriction is applied to each Group.

Applicant is advised that examination will be restricted to only the elected antigen and should not be construed as a species election.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups I-V appear to be genes of *Streptococcus pneumoniae*. However, Biswas et al. (U.S. Patent 6,303,771 B1) disclose an invention which relates to pth, peptidyl tRNA hydrolase, of *Streptococcus pneumoniae* (see column 2, lines 1 and 61-63).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Helen Lee on November 30, 2008 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-3. Ms. Lee further elected knock out gene SP0005. Affirmation of this election must be made by applicant in replying to this Office action.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claims 1-10 are pending. Claims 8-10 have been added. Claims 3, 6 and 7 have been amended. Claims 4-10 have been withdrawn from further consideration as being drawn to non-elected inventions. Claims 1-3 are currently under examination. Claims 1-3 will only be examined to the extent that the claims pertain to the elected knock out gene SP0005.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on February 08, 2006 is in compliance with the provisions of 37 CFR 1.97 and has been considered. An initialed copy is attached hereto.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

3. Claims 1 is objected to because of the following informalities: 1) "Pneumoniae" should be spelled with a lower case 'P', as pneumoniae is the species, 2) Claim 1 recites limitations of non-elected and withdrawn inventions and 3) Claim 1 recite the use of an NPL reference, this is inappropriate use of said reference.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out, wherein the SPnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain in Tettelin et al.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus of antigens or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession of the claimed invention.

A representative number of species means that the species which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure

or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

The specification does not provide substantive evidence to describe a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out and as a result has the SPnnnn nomenclature that refers to the gene numbering assigned to *S. pneumoniae* TIGR4 strain, lead alone the strain referred to in Tettelin et al. (2001) Science 293:498-506. The specification is silent with regard to how an isogenic deletion of the coding region is accomplished. The specification is equally silent with regard to which Spnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain in Tettelin et al. The specification is silent with regard to the specific structure associated with the laboratory designation SP0005 and as such written description is lacking.

Moreover, the specification discloses that knockout of any of the 91 genes, which include SP0005 resulted in no growth and is lethal (see Table 1, pages 28 and 29). The specification does not describe any use of a dead bacteria, which appears to be the only thing knocking out the SP0005 gene would accomplish.

The University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: ...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v.

American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

Further, Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

5. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled.

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CRFC1988). The Wands factors have been considered in the establishment of this scope of enablement rejection. These factors include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claimed invention is directed to a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out, wherein the SPnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae*TIGR4 strain in Tettelin et al.

Breadth of the claims: The specification does not provide support for the claims as they are broadly drawn and encompass an unknown nomenclature.

Direction or guidance presented in the specification: The specification does not provide substantive evidence to describe a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out and as a result has the SPnnnn nomenclature that refers to the gene numbering assigned to *S. pneumoniae* TIGR4 strain, lead alone the strain referred to in Tettelin et al. (2001) Science 293:498-506. The specification is silent with regard to how an isogenic deletion of the coding region is

accomplished. The specification is equally silent with regard to which Spnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain in Tettelin et al.

Moreover, the specification disclose that knockout of any of the 91 genes, which include SP0005 resulted in no growth and is lethal (see Table 1, pages 28 and 29). The specification does not describe any use of a dead bacteria, which appears to be the only thing knocking out the SP0005 gene would accomplish. The specification does not disclose how to use the invention as claimed.

Presence or absence of working examples: There are no working examples provided to rectify the missing information in the instant specification pertaining to the claimed invention.

Quantity of experimentation necessary: The quantity of experimentation necessary would be undue as the claims encompass unspecified nomenclature. The specification is silent with regard to the specific structure associated with the laboratory designation SP0005 and as such enablement is lacking. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to make/use the claimed genus. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of

guidance and working examples provided in the specification and the high degree of unpredictability as evidence by the state of the prior art, attempting the construct and test variants of the claimed invention would constitute undue experimentation.

6. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The SPnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain, which is critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). Claims have incorporated that the SPnnnn nomenclature refers to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain as described in Tettelin et al. (2001) Science 293: 498-506.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the use of the terms "SPnnnn nomenclature". It is unclear what is meant by said terms, as it is not explicitly defined in the specification. What constitutes a "SPnnnn nomenclature"? As written, it is

impossible to determine the metes and bounds of the claimed invention.

Claim 1 is rendered vague and indefinite by the use of the terms "isogenic deletion". It is unclear what is meant by said terms, as it is not explicitly defined in the specification. What constitutes an "isogenic deletion"? As written, it is impossible to determine the metes and bounds of the claimed invention.

8. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: that in claim 1 the elected gene is described by a laboratory designation that conveys no structure as it refers to a non-patent literature article.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Biswas et al. (U.S. Patent 6,303,771 B1).

The rejected claims are drawn to a *Streptococcus pneumoniae* bacterium in which expression of SP0005 has been knocked out, wherein the SPnnnn nomenclature

refers to the gene numbering assigned to the *S. pneumoniae*TIGR4 strain in Tettelin et al.

Biswas et al. disclose an invention which relates to pth, peptidyl tRNA hydrolase, of *Streptococcus pneumoniae* (see column 2, lines 1 and 61-63). The specification discloses that the TIGR4 annotation for SP0005 is pth (see page 29; Table 1). Biswas et al. disclose that polynucleotide's encoding pth variants are substituted, modified, deleted, and/or added (see column 10, lines 37-44). Moreover, Biswas et al. disclose that a marker sequence that facilitates purification of the fused polypeptide can be coded (see column 9, lines 31-34). The bacterium of Biswas is identical to the instantly claimed invention, it necessarily has the SPnnnn nomenclature to the gene numbering assigned to the *S. pneumoniae* TIGR4 strain in Tettelin et al.

Since the Office does not have the facilities for examining and comparing applicants' composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKIA J. TONGUE whose telephone number is

(571)272-2921. The examiner can normally be reached on Monday-Friday 8-5:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LJT

12/16/08

/Robert A. Zeman/
for Lakia J. Tongue, Examiner of Art Unit 1645